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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : DeBrabander *et al.* Customer No.: 21003  
Serial No. : 10/783,848 Examiner: Not Yet Assigned  
Filed : February 20, 2004 Group Art Unit: 1614  
For : SYNTHESIS OF PELORUSIDE A AND ANALOGS THEREOF FOR  
USE AS ANTITUMOR AGENTS

INFORMATION DISCLOSURE STATEMENT

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

November 17, 2004  
Date of Deposit

Rochelle K. Seide  
Attorney Name  
Rochelle K. Seide  
Signature

32,300  
Patent Reg. No.  
November 17, 2004  
Date of Signature

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. §§1.97 and 1.98, Applicants respectfully request that the documents listed below in reverse chronological order and on the accompanying PTO Form 1449 be considered by the Examiner and made of record in the above-referenced application. Copies of the document listed are enclosed.

1. U.S. Patent Publication No. US 2002/0193423 by Peter T. Northcote et al., published December 19, 2002.
2. Hood et al. (2002) "Peloruside A, a novel antimitotic agent with paclitaxel-like microtubule-stabilizing activity", *Cancer Research* 62: 3356-3360.
3. Smith et al. (2002) "Total Syntheses of (+)-Zampanolide and (+)-Dactylolide exploiting a unified strategy", *J. Am. Chem. Soc.* 124: 11102-11113.
4. Ahn et al. (2002) "An approach to the stereoselective synthesis of *syn*- and *anti*-1,3-diol derivatives. Retention of configuration in the Mitsunobu reaction", *J. Org. Chem.* 67: 1754-1759.
5. International PCT Publication No. WO 01/10869, published February 15, 2001.
6. Hood et al. (2001), "The novel cytotoxic sponge metabolite peloruside A, structurally similar to bryostatin-1, has unique bioactivity independent of protein kinase C", *Anti-Cancer Drug Design*, 16: 155-166.
7. Smith et al. (2001) "Total synthesis of (+)-phorboxazole A exploiting the Petasis-Ferrier rearrangement", *J. Am. Chem. Soc.*, 123: 10942-10953.
8. West et al. (2000) "Peloruside A: a potent cytotoxic macrolide isolated from the New Zealand marine sponge *Mycale* sp", *J. Org. Chem.* 65: 445-449.
9. Chatterjee et al. (2000) "Synthesis of functionalized olefins by cross and ring-closing metatheses", *J. Am. Chem. Soc.* 3783-3784.
10. Evans et al. (1999) "Total synthesis of bryostatin 2", *J. Am. Chem. Soc.* 121: 7540-7552.
11. Wender et al. (1998) "Synthesis of the first members of a new class of biologically active bryostatin analogues", *J. Am. Chem. Soc.*, 120: 4534-4535.

12. Corey et al. (1998) "reduction of carbonyl compounds with chiral oxazaborolidine catalyst: a new paradigm for enantioselective catalysis and a powerful new synthetic method", *Angew. Chem. Int. Ed.* 37: 1986-2012.
13. Xu et al. (1997) " Applications of Zr-catalyzed carbomagnesation and Mo-catalyzed macrocyclic ring closing metathesis is assymetric synthesis. Enantioselective total synthesis of Sch 38516 (Fluvirucin B<sub>1</sub>)", *J. Am. Chem. Soc.* 119: 10302-10316.
14. Giannakakou et al. (1997) "Paclitaxel-resistant human ovarian cancer cell have mutant beta-tubulins that exhibit impaired paclitaxel-driven polymerization", *J. Biol. Chem.*, 272: 17118-17125.
15. Evans et al. (1996) "A stereochemical model for merged 1,2- and 1,3-asymmetric induction in diastereoselective mukaiyama aldol addition reactions and related precesses", *J. Am. Chem. Soc.* 118: 4322-4343.
16. Smith et al. (1993) "Total synthesis of calicheamicin  $\gamma_1^1$ . Development of an enantioselective route to (-)-calicheamicinone", *J. Am. Chem. Soc.* 115: 7612-7624.
17. Rychnovsky et al. (1993) "Analysis of two <sup>13</sup>C NMR correlations for determining the stereochemistry of 1,3-diol acetonides", *J. Org. Chem.* 58: 3511-3515.
18. Kageyama et al. (1990) "Synthesis of bryostatin 7", *J. Am. Chem. Soc.* 112: 7407-7408.
19. Skehan et al. (1990) "New colorimetric cytotoxicity assay for anticancer-drug screening", *J. Natl. Cancer Inst.*, 82(13): 1107-12.
20. Brown et al. (1988) "Chiral synthesis via organoboranes. A. highly diastereoselective and addition of [(Z)- $\gamma$ -alkoxyallyl]diisopinocampheylboranes to aldehydes", *J. Am Chem. Soc.* 110:1535-1538.

21. Oyo Mitsunobu (1981) "The use of diethyl azodicarboxylate and triphenylphosphine in synthesis and transformation of natural products", *Synthesis* 1-28.
22. Still et al. (1978) "Rapid chromatographic technique for preparative separations with moderate resolution", *J. Org. Chem.*, 43: 2923-2925.
23. Luche et al. (1978) "Reduction of natural enones in the presence of cerium trichloride", *J. Chem. Soc., Chem. Commun.*: 601-602.

Identification of the listed documents is not to be construed as an admission of the applicants or attorneys for applicants that such citations are available as "prior art" against the subject application. If the Examiner applies the documents as prior art against any claim in the application and applicants determine that the cited documents do not constitute "prior art" under United States law, applicants reserve the right to present to the Office the relevant facts and law regarding the appropriate status of the documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should the documents be applied against the claims of the present application.

This Information Disclosure Statement is being filed before the mailing date of the first Office Action on the merits of referenced application. Therefore, Applicants do not believe that any fee is due in connection with the submission of this paper. However, if any fee is due, or if any overpayment has been made, the Commissioner is authorized to charge any such fee or credit any overpayment, to our Deposit Account No. 02-4377. Duplicate copies of this sheet are enclosed.

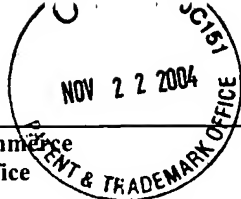
Respectfully submitted,  
BAKER BOTTS L.L.P.



Rochelle K. Seide  
PTO Reg. No. 32,300  
*Attorney for Applicants*

Dana Lau  
PTO Reg. No. 55,361  
*Agent for Applicants*

30 Rockefeller Plaza  
44th Floor  
New York, NY 10012-4498  
(212) 408-2500

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AP35699 - 090495.0282Serial No.  
10/783,848**INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT**  
(Use several sheets if necessary)Applicants  
DeBrabander et al.Filing Date  
February 20, 2004Group Art Unit  
1614**U.S. PATENT DOCUMENTS**

*Ex am. Ini t.	Document No.	Date	Name	Class	Subclass	Filing Date if Appropriate

**FOREIGN PATENT DOCUMENT**

Document No.	Date	Name	Class	SubClass	Translator Yes No
0 1 1 0 8 6 9	02/15/01	WO			

**OTHER DOCUMENTS (including Author, Title Date, Pertinent Pages, Etc.)**

	U.S. Patent Publication No. US 2002/0193423 by Peter T. Northcote et al., published December 19, 2002.
	Hood et al. (2002) "Peloruside A, a novel antimetabolic agent with paclitaxel-like microtubule-stabilizing activity", <i>Cancer Research</i> <b>62</b> : 3356-3360.
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	Chatterjee et al. (2000) "Synthesis of functionalized olefins by cross and ring-closing metatheses", <i>J. Am. Chem. Soc.</i> <b>122</b> : 3783-3784.

Examiner

Date Considered

\* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 U.S. Department of Commerce  
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